L35 ANSWER 167 OF 272 HCAPLUS COPYRIGHT 2006 ACS on STN
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DOCUMENT NUMBER: 122:188019
TITLE: Preparation of substrate-spacer-active substance prodrugs
INVENTOR(S): Bosslet, Klaus; Czech, Joerg; Hoffmann, Dieter; Kolar, Cenek; Tillequin, Francois; Florent, Jean Claude; Azoulay, Michel; Monneret, Claude; Jacquesy, Jean Claude; et al.
PATENT ASSIGNEE(S): Behringwerke AG, Germany
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CODEN: GWXXBX
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FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

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DE 4236237	A1	19940428	DE 1992-4236237	19921027
EP 647450	A1	19950412	EP 1993-114475	19930909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 595133	A2	19940504	EP 1993-116702	19931015
EP 595133	A3	19981104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
IL 107398	A1	20010128	IL 1993-107398	19931025
CA 2109259	AA	19940428	CA 1993-2109259	19931026
CA 2109259	C	20050524		
NO 9303854	A	19940428	NO 1993-3854	19931026
NO 311830	B1	20020204		
AU 9350225	A1	19940512	AU 1993-50225	19931026
AU 669218	B2	19960530		
JP 06293665	A2	19941021	JP 1993-266976	19931026
ZA 9307951	A	19950705	ZA 1993-7951	19931026
US 5955100	A	19990921	US 1995-449021	19950524
US 6146658	A	20001114	US 1997-859084	19970520

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US 1993-140825 A3 19931025
US 1995-449021 A1 19950524

AB Compds. of the form substrate-spacer-active substance, where the substrate and spacer are cleaved under physiol. or pathophysiol. conditions, the substrate is not an amino acid or peptide residue, and the active ingredient is a chemical compound with biol. activity or a derivative thereof, with the exception of N-bonded derivs. of anthracycline, paranitroanilide, or cytosine arabinoside, were prepared Thus, 3'-N-fluorenylmethoxycarbonyldoxorubicin in PhMe was treated with diisopropylethylamine and diphosgene; after 1 h 4-(6-O-methyl-β-D- glucuronyloxy)-3-nitrobenzylamine and diisopropylethylamine in DMF were added and the mixture was stirred 14 h to give, after deprotection, 14-O-[4-(β-D-glucuronyloxy)-3-nitrobenzylaminocarbonyl]doxorubicin (I). I showed an acute LD50 in mice of >1500 mg/kg, vs. 20 mg/kg for doxorubicin itself. I at 500 mg/kg in mice implanted with human LOVO colon tumors showed a T/C = 40.0%.

IT **59865-13-3DP**, Cyclosporin a, substrate-spacer prodrugs of
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of)
RN 59865-13-3 HCAPLUS
CN Cyclosporin A (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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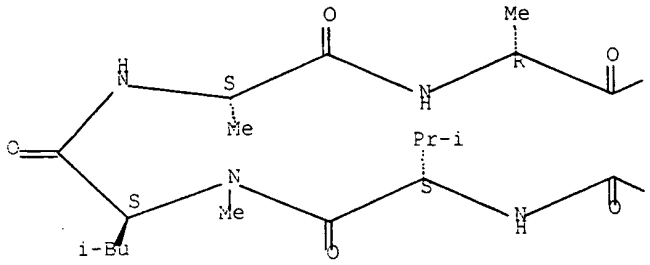

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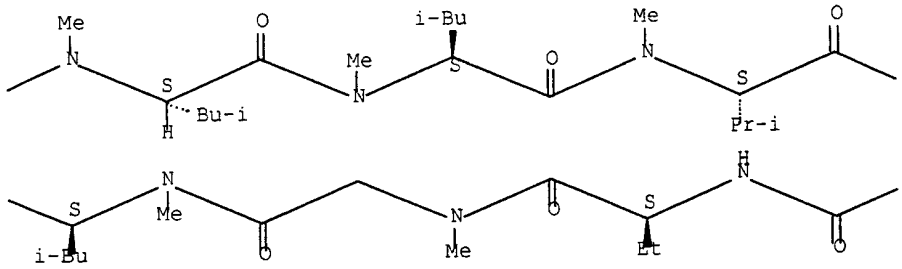

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